

# Chapter 3 EPA's Risk Assessment Process for Air Toxics: History and Overview

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### 3.1 Introduction

This chapter provides the historical backdrop to the air toxics risk assessment process that is in use at EPA today. It examines the overall framework of the risk assessment process and how the various elements of the process relate to one another, including resource and timing considerations. Subsequent chapters of this reference manual describe each of the specific elements of the risk assessment process in detail.

### 3.2 A Short History of the Development of Human Health Risk Assessment and Risk Management Approaches for Air Toxics

Risk assessment is not new. However, only recently have some attempted to formalize the process into a coherent framework. This section briefly describes the chronology and important events in the development of those risk assessment methodologies outlined in this document.

#### 3.2.1 The 1983 National Academy of Sciences Report

In the 1980s, the emerging practice of federal-level risk assessment spurred Congress to commission a report from the National Research Council (NRC) of the National Academy of Sciences (NAS) on how the process was being used. The result was the landmark 1983 study entitled *Risk Assessment in the Federal Government: Managing the Process*.<sup>(1)</sup>

The document is often referred to as “The Red Book” because of its distinctive red cover. The Red Book acknowledged that regulatory agencies have differing statutory obligations that require some flexibility in both the risk assessment and risk management processes. The Red Book also clarified what risk assessment and risk management are by giving them the definitions that are still commonly used today (see Exhibit 3-1):

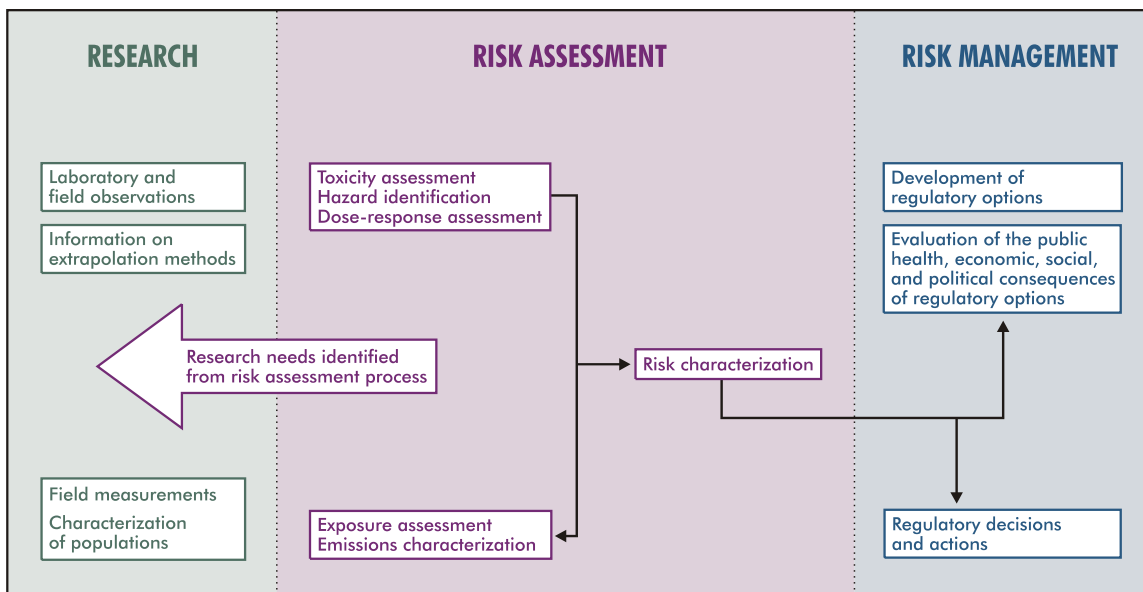
#### Purpose of the 1983 NRC Report

- Assess the merits of separating the analytic functions of developing risk assessments from the regulatory functions of making policy decisions.
- Consider the feasibility of designating a single organization to do risk assessments for all regulatory agencies.
- Consider the feasibility of developing uniform risk assessment guidelines for use by all regulatory agencies.



- “We use **risk assessment** to mean the characterization of the potential adverse health effects of human exposures to environmental hazards” (p. 18).
- “The Committee uses the term **risk management** to describe the process of evaluating alternative regulatory actions and selecting among them” (p. 18).

### Exhibit 3-1. Risk Assessment and Risk Management Paradigm



Source: Adapted from the 1983 “Red Book”

The Red Book did not recommend “bright line analysis” because it gives too much weight to risk numbers that are, by their very nature, uncertain. The NRC also made two important recommendations regarding the risk assessment and risk management processes used by federal agencies:

- First, the scientific finding and policy judgments embodied in risk assessments should be explicitly distinguished from the political, economic, and technical considerations that influence the design and choice of regulatory strategies.
- Second, uniform guidelines should be developed for use by federal regulatory agencies in the risk assessment process.

#### Bright Line Analysis

“Bright line analysis” is the process of comparing a risk assessment result (the estimated numerical value of risk) to a preestablished acceptable level of risk (the “bright line”) and making risk management decisions solely on whether the estimated risk is above or below the acceptable level. The NRC emphasized that risk assessment results are only one component of the risk management decision process and that assessment results should not be the only information risk managers consider.

The Red Book had a significant impact on risk assessment and management processes throughout the federal government, and it continues to be an influential reference at EPA. For example, in response to its recommendations, EPA established the Risk Assessment Council (RAC) and began publishing Agency-wide risk assessment guidelines (see Section 3.1.4 below). (Note that the recommendation to develop uniform risk assessment guidelines for use by all regulatory agencies did not happen – each agency is still free to develop their own approaches and guidelines.)

### 3.2.2 The 1994 National Research Council Report

Recognizing the growing importance of quantitative risk assessment in the regulatory process, Congress in section 112(o) of the Clean Air Act (CAA) amendments required EPA to enter into a contract with the NRC to evaluate the risk assessment methods EPA was using at the time. The NRC's 1994 report, *Science and Judgment in Risk Assessment*,<sup>(2)</sup> was prepared by the NRC's Committee on Risk Assessment of Hazardous Air Pollutants in the Board on Environmental Studies and Toxicology. In a sense, the "Blue Book" was a follow-up to the 1983 Red Book, but with a specific emphasis on EPA's scientific methods.

#### Purpose of the 1994 NRC Report

Congress asked the NRC to answer the following questions:

- Given that quantitative risk assessment is essential for EPA's implementation of the CAA, is EPA conducting risk assessments in the best possible manner?
- Has EPA developed mechanisms for keeping its risk assessment procedures current in the face of new developments in science?
- Are adequate risk-related data being collected to permit EPA to carry out its mandates?
- What, if anything, should be done to improve EPA's development and use of risk assessments?



The NRC committee observed that several themes were common to all elements of the risk assessment process and noted that these themes were usually the focal points for criticisms of individual risk assessments:

- The use of default assumptions;
- Available data;
- Uncertainty and variability;
- Assessment of multiple chemical exposures, multiple routes of exposure, the potential for multiple adverse effects; and
- Steps taken to validate the methodologies used throughout the risk assessment process.

In the Blue Book, the NRC updated the risk assessment/risk management paradigm and presented several recommendations for increasing the effectiveness and accuracy of EPA's risk assessment and risk management process, particularly as it pertained to air toxics:

- EPA should generally retain its conservative, default-based approach to risk assessment for screening analysis in standard-setting.
- EPA should use iterative approaches that incorporate improvements in both the models and data used in each successive iteration of analysis. For example, EPA should start with relatively inexpensive screening techniques and move to a more resource-intensive level of data-gathering, model construction, and model application as the particular situation warrants. This method avoids costly case-by-case evaluations of individual chemicals at every facility in every source category.

- EPA should explicitly identify each use of a default option in a risk assessment, should clearly state the scientific and policy basis for each default option, and should consider attempting to give greater formality to its criteria for departure from default options.
- EPA should establish regulatory priorities based on initial assessments of each chemical's possible impact on human health and welfare.
- EPA should present not only point estimates of risk, but also the sources and magnitudes of uncertainty associated with these estimates.

EPA has progressively worked to adopt the report's recommendations as it transitions the Agency into the risk-based phase of the CAA legislative strategy for HAPs.

### 3.2.3 The CRARM

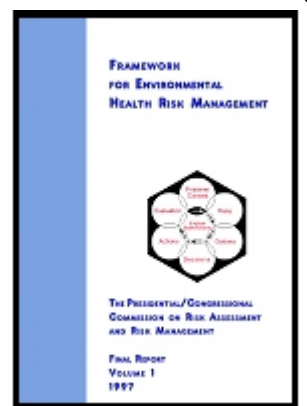
Section 303 of the 1990 CAA Amendments mandated the formation of a Presidential Commission on Risk Assessment and Risk Management (CRARM) in response to unresolved questions about EPA's approach to assessing public health risks remaining after implementation of the maximum achievable control technology (MACT) program (i.e., technology based control).

CRARM released its report, *Risk*

*Assessment and Risk Management in Regulatory Decision-Making*, or the White Book, in two volumes in 1997. Volume I focuses on the framework for environmental health risk management. Volume II addresses a variety of technical issues related to risk assessment and risk management, including a common metric for assessment of cancer and other effects, management of residual risks from air toxics, comparative risk, decision criteria, uncertainty analysis, and recommendations to specific agencies.<sup>(3)</sup>

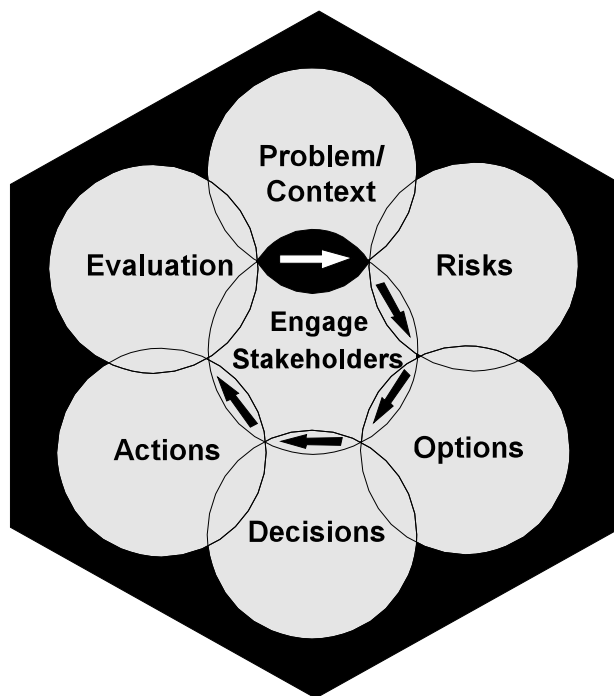
#### Purpose of the 1997 White Book

Investigate "the policy implications and appropriate uses of risk assessment and risk management in regulatory programs under various Federal laws to prevent cancer and other chronic health effects which may result from exposure to hazardous substances."



The CRARM developed a risk management framework that fosters an integrated approach to addressing complex, real-world issues that affect multiple environmental media and involve exposures to mixtures of chemicals (Exhibit 3-2). Note that risk assessment (here "risk") is one of several steps in risk management. The framework aims to encourage integrated approaches to environmental risk management.

**Exhibit 3-2. The CRARM Framework for Risk Management**



The central element of the framework is encouraging stakeholder participation throughout the six stages of risk management. In addition, the framework intends to be iterative – if appropriate, risk assessors can redefine and reassess the risk problem as they develop new data. Another key principle of the framework is that risk management should explicitly consider the comprehensive, real-world context of a risk problem and not limit the context to one that considers only one type of risk associated with a single chemical in a single environmental medium. The CRARM made several additional recommendations:

- **Conduct Comparative Risk Assessment.** Federal agencies should try a comparative risk analysis approach on an experimental or demonstration basis to seek consensus on priorities for managing environmental risks. The results of such efforts should influence agency resource allocation.
- **Harmonize Cancer and Non-Cancer Methodologies.** Assessment techniques for carcinogens and non-carcinogens should be harmonized. This would aid in risk communication, risk management decisions, and comparative risk assessment.
- **Devise Realistic Exposure Scenarios.** Risk management decisions should be based on realistic exposure scenarios, rather than on the hypothetical **maximum exposed individual** (MEI). Distributions of the varied exposures within a population should be evaluated with

explicit attention to specific segments of the population (e.g., individuals with unusually high exposures, infants, children, pregnant women, low-income groups, and minority communities with exposures influenced by social or cultural practices).

- **Place Cost-Benefit Analysis in its Appropriate Context.** Economic analysis is a relevant consideration in risk management decisions, but should not be the overriding factor in a decision. Explicit descriptions of assumptions, data sources, sources of uncertainty, and costs across society should be presented in parallel with descriptions associated with risk assessments.
- **Ensure Interagency Consistency.** Agencies should coordinate their risk assessment methods and assumptions unless there is a specific statutory requirement that allows for different choices. Scientific disagreements should be explained.
- **Conduct Tiered Residual Risk Assessments.** EPA should implement a tiered approach to managing residual risks after implementation of the CAA's technology-based (MACT) standards.

Similar to the recommendations outlined in the Blue Book, EPA has continued to modify its risk assessment guidelines and approaches in response to these recommendations. Other documents, such as the National Research Council's 1996 document entitled *Understanding Risk: Information Decisions in a Democratic Society*,<sup>(4)</sup> also play a role in informing the continued development of the risk assessment and risk management process.<sup>(a)</sup>

### 3.2.4 Development of Human Health Risk Assessment at EPA

EPA has conducted human health risk assessments since its inception in 1970. EPA built on this early experience while confronting potential hazards associated with pesticide use. For example, after considering available human and non-human toxicity data, EPA restricted domestic use of DDT and other pesticides, in part due to their cancer risks.

EPA acknowledged that such risk-based regulations needed an appropriate scientific basis and began collecting cancer toxicity information on pesticides through administrative hearings and testimony.

Summary documents from these hearings became known as the "Cancer Principles." Criticism of these documents, which many inadvertently perceived to be formal Agency cancer risk assessment policy, led the Agency to develop interim guidelines in 1976. Three years later, the

#### Fundamental References for Air Toxics Risk Assessment

- (1) Air Toxics Risk Assessment Reference Library, three volumes
  - (2) The NAS Red and Blue Books
  - (3) CRARM White Book
  - (4) EPA Guidelines for Risk Assessment Series
- (Full citations are at the end of this chapter.)

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<sup>a</sup>*Understanding Risk* "...illustrates that making risks understandable to the public involves more than translating scientific knowledge. The volume also draws conclusions about what society should expect from risk characterization and offers guidelines and principles for informing the wide variety of risk decisions that face our increasingly technological society." (See <http://books.nap.edu/catalog/5138.html>.)

Interagency Regulatory Liaison Group (a conglomeration of several federal agencies, including EPA) published additional cancer risk assessment guidelines. Concurrently, EPA used cancer risk assessment techniques in its toxic chemicals regulation under the 1976 Toxic Substances Control Act. By the end of EPA's first decade in existence, the Agency used risk assessment techniques to develop water quality criteria protective of human health.

Throughout the 1980s, EPA increasingly utilized risk assessment to evaluate the potential for chemicals to cause non-cancer health effects in addition to cancer risks. During the 1980s, the Agency used cancer risk assessment techniques in the development of national emission standards for air toxics such as vinyl chloride and benzene.

As EPA increased its use of risk assessment throughout the 1980s, the Agency's inconsistent approach to risk assessment became apparent, largely due to a lack of standard guidance on the topic. To correct this problem, the Agency undertook administrative reforms and published several key guidelines and other policy documents.

First, the Agency published *Risk Assessment and Management: Framework for Decision Making*.<sup>(5)</sup> EPA intended this reference manual to conform EPA practices with NRC Red Book recommendations and to help the Agency make better and more rapid decisions about environmental toxic chemical problems.

Next, in 1986, EPA established the *Risk Assessment Council* (RAC) to oversee virtually all aspects of the Agency's risk assessment process. EPA appointed Senior Agency officials with experience and responsibilities in the area of science policy and risk assessment to the RAC. This group established EPA's fundamental policies for conducting risk assessments and evaluating risk information. These officials also oversaw the activities of the Risk Assessment Forum.

Subsequently, EPA began publishing an influential series of Agency-wide guidelines in the *Federal Register* identifying the recommended methods for assessing human health risks from environmental pollution. EPA did not intend for these guidelines, which cover both cancer risks and non-cancer hazards, to be static, and the Agency has revised the guidelines as new information and methods become available (for example, EPA began a process in 1996 to revise and update its guidelines for carcinogenicity).

#### **EPA Risk Assessment Forum**

The Risk Assessment Forum is a standing committee of senior EPA scientists established to promote Agency-wide consensus on difficult and controversial risk assessment issues and to ensure that this consensus is incorporated into appropriate Agency risk assessment guidance. To fulfill this purpose, the Forum assembles Agency risk assessment experts in a formal process to study and report on issues from an Agency-wide scientific perspective. Major Forum guidance documents are developed in accordance with the Agency's regulatory and policy development process and become Agency policy upon approval by the Administrator or the Deputy Administrator. Risk Assessment Forum products include: risk assessment guidelines, technical panel reports on special risk assessment issues, and peer consultation and peer review workshops addressing controversial risk assessment topics

(<http://cfpub.epa.gov/ncea/raf/index.cfm>).

EPA established the Science Policy Council (SPC) in 1993 with a broader mission and as a replacement for the RAC; specifically, the SPC aims to integrate policies that guide Agency decision-makers in their use of scientific and technical information. To accomplish this goal, the SPC works to implement and ensure the success of selected initiatives that external advisory bodies (such as the National Research Council and the Science Advisory Board, as well as others such as the Congress, industry and environmental groups, and Agency staff), recommend. In this way, the SPC provides guidance for selected EPA regulatory and enforcement policies and decisions. The 1995 Guidance for Risk Characterization was an important part of the SPC's risk characterization program. Standing groups such as the Risk Assessment Forum, a Steering Committee, and interim working groups continue to support the SPC. For more information on the SPC, see <http://www.epa.gov/osp/spc/2about.htm>.

#### **EPA Human Health Risk Assessment Guidelines<sup>a</sup>**

##### **Carcinogenicity**

- 1999 Draft Revised Guidelines for Carcinogen Risk Assessment<sup>b</sup>
- 1986 Guidelines for Carcinogen Risk Assessment

##### **Chemical mixtures**

- 2000 Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures
- 1986 Guidelines for the Health Risk Assessment of Chemical Mixtures

##### **Developmental toxicity**

- 1991 Guidelines for Developmental Toxicity Risk Assessment

##### **Exposure assessment**

- 1992 Guidelines for Exposure Assessment

##### **Mutagenicity**

- 1986 Guidelines for Mutagenicity Risk Assessment

##### **Neurotoxicity**

- 1998 Guidelines for Neurotoxicity Risk Assessment

##### **Probabilistic analysis**

- 1997 Guiding Principles for Monte Carlo Analysis

##### **Reproductive toxicity**

- 1996 Guidelines for Reproductive Toxicity Risk Assessment

##### **Risk characterization**

- 2000 Handbook for Risk Characterization
- 1997 Guidance on Cumulative Risk Assessment. Part 1, Planning and Scoping
- 1995 Guidance for Risk Characterization

<sup>(a)</sup> A current list is available at <http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=55907>.

<sup>(b)</sup> These guidelines are interim final drafts. Check above website for a final version.

Another important group within EPA with a risk assessment focus is the National Center for Environmental Assessment (NCEA). NCEA is a major component of the EPA's Office of Research and Development and acts as EPA's national resource center for human health and ecological risk assessment. NCEA conducts risk assessments, carries out research to improve the state-of-the-science of risk assessment, and provides guidance and support to risk assessors. Many of the critical Agency documents on risk assessment science and policy, as well as risk related databases such as the Integrated Risk Information System (IRIS), can be accessed through the NCEA website ([www.epa.gov/ncea](http://www.epa.gov/ncea)).

EPA's use and development of human health risk assessment continued to grow through the 1980s and 1990s with establishment of the IRIS toxicity database, the Agency's repository of chemical-specific toxicity data. IRIS is a critical resource for risk assessors because the database contains toxicity information that reflects a consensus among EPA program offices about a chemical's toxic properties.

EPA's Office of Solid Waste and Emergency Response's Superfund Program also has developed a series of very detailed guidance documents to help risk assessors understand the actual nuts-and-bolts of performing human and ecological risk assessments under the Superfund program. These "how to" documents are called the ***Risk Assessment Guidance for Superfund*** series, or the RAGS series for short. RAGS provides in-depth discussions and guidance for risk assessors to use in their day-to-day work and is an important reference for those working in the field of risk assessment.<sup>(b)</sup> A full set of RAGS documents is available online.<sup>(6)</sup>

**Risk Assessor.** The individual or team of individuals who organizes and analyzes air toxics data, develops exposure and risk calculations, and prepares the human health risk assessment reports. Risk assessors for air toxics can be industry, EPA, an S/L/T air agency, or contractor personnel. The larger **risk assessment team** will often be made up of people with a variety of expertise, including health scientists, monitoring or modeling personnel, and laboratory analysts.

**Risk Manager.** The individual or group of individuals who serve as the primary decision maker(s) for an area subject to the risk analysis process. The risk managers may base their decisions about the need for risk reduction on a variety of data, including the results of the risk assessment, economic considerations, technical feasibility of risk reduction options, community acceptance, and a number of other factors.

### 3.3 Air Toxics Human Health Risk Assessment: Overview of the Process

The reports and guidance documents discussed above tend to distill the risk assessment process down to the following five questions:

- Who is exposed to environmental pollutants?
- What pollutants are they exposed to?
- How are they exposed?
- How toxic are the chemicals they are exposed to?
- What is the likelihood that harm will occur because of the exposures?

The role of the risk assessor is to answer these questions. The main product of the risk assessment is a set of qualitative and quantitative statements about the likelihood that people will experience adverse health outcomes because of the exposures. The statements also should discuss how certain the assessor is about these statements. **Risk managers** then use the risk assessment results and other relevant information (including the cost or technical feasibility of resolving a problem) to decide what (if anything) should be done to reduce risk.

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<sup>b</sup>Although the information provided in RAGS is primarily geared towards Superfund sites, some of these procedures are generally relevant and compatible to risk assessments developed by other Program Offices, including the Office of Air and Radiation. As such, the information provided in RAGS was taken into consideration in the development of this reference library.

The following sections briefly describe the overall risk assessment process for releases of air toxics to the ambient air. Subsequent chapters of this reference manual revisit each of these subjects in detail and provide contacts and references for more information.

### 3.3.1 Air Toxics Risk Assessment: What Is the Question?

The overall purpose of a human health air toxics risk assessment is to attempt to understand public health risks potentially associated with exposures to particular pollutants emitted into the air from sources of interest. Exhibit 3-3 presents a simple illustration of the overall real-world process that is investigated through the use of risk assessment.

As Exhibit 3-3 illustrates, air toxics risk assessments usually focuses, at a minimum, on the inhalation of contaminated air. However, for a small subset of air toxics (discussed in Chapter 4), the risk assessment also may need to address ingestion of or dermal contact with soils, water, or food that have become contaminated with chemicals that have deposited out of the air. (Dermal exposures are included here for completeness, but usually they are less of a risk factor for air toxics than ingestion or inhalation exposures.)

The following simple mathematical formula describes the basis for human health risk assessment. Specifically, the likelihood that injury or disease may occur from exposure to air toxics can be described as a function of two separate, but related, things – an estimate of exposure to a chemical and an estimate of the toxic properties of the chemical:

$$\begin{aligned} &\text{Potential for Injury or Disease (i.e., the "Risk")} \\ &= f(\text{metric of exposure, metric of toxicity})^{(c)} \end{aligned} \quad (\text{Equation 3-1})$$

Two key principles emerge from this formula and Exhibit 3-3:

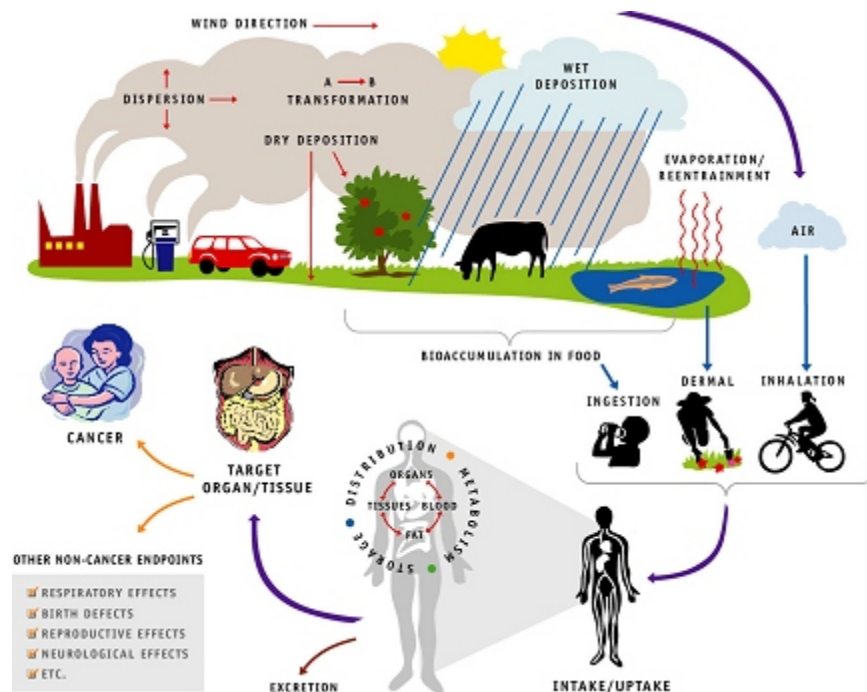
- **There is no risk if there is no exposure.** If a person has no chance of coming in contact with an air toxic, the risk posed to that person is zero.
- **The level of risk associated with an exposure depends on the toxic properties of the chemical.** These properties determine whether the exposure is of great or little concern. Some chemicals can cause severe health effects (even death) when a person receives exposure even to extremely small quantities at a single point in time. Conversely, other chemicals cause essentially no effect even after repeated exposure to high levels over long periods of time.

The general Equation 3-1 is important to understand and keep in mind since the exact equations used to develop risk estimates are derived from it. In other words, the risk equations that will be detailed in later chapters all include both a estimate of exposure and an estimate of toxicity.

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<sup>c</sup>The symbol “f” means “is a function of”

### Exhibit 3-3. Generic Conceptual Model of How Air Toxics Releases May Result in Injury or Disease



Starting at the upper left hand side of this diagram, air toxics are released from one or more sources (e.g., factories, cars/trucks, small businesses, forest fires) to the air and begin to disperse by the wind away from the point of release. Once released, the chemical may remain airborne; convert into a different substance; and/or deposit out of the air onto soils, water, or plants. People may be exposed to air toxics by breathing contaminated air (inhalation) or through ingestion of chemicals that can accumulate in soils, sediments, and foods (the latter process is called **bioaccumulation**). People also can be exposed to deposited chemicals via skin (dermal) contact, however, this tends to be a less important risk factor than ingestion or inhalation. Inhalation, ingestion, and dermal absorption are called the **routes of exposure**.

This description of what happens to an air toxic once it is released into the air is called **fate and transport** analysis. “Transport” evaluates how an air toxic physically moves (i.e., is transported) through the environment. “Fate” describes what ultimately happens to the chemical after it is released to the air (i.e., what is the “fate” of the chemical in the environment). The results of a fate and transport analysis is an estimate of the concentration of the air toxic in the air, soil, water, and/or food at the point where it is contacted by a person. The **exposure assessment** is the process of evaluating how human contact with the contaminated media occurs.

In the case of an air pathway analysis, the metric representing the inhalation exposure is called the **exposure concentration** (EC). For example, if benzene is released from a factory and blows into a nearby neighborhood where people breath it, the EC is the concentration of benzene in the air that they breath.

Once an exposure occurs, the air toxics can enter the body and exert an effect at the point of entry (the “portal of entry”) or move via the bloodstream to other target organs or tissues. The action of a pollutant on a target organ can result in a variety of harmful effects, including cancer, respiratory effects, birth defects, and reproductive and neurological disorders. An overall risk assessment process evaluates what people are exposed to, how the exposure occurs, and, when combined with information about the toxic properties of the chemicals in question, estimates the likelihood that the exposure will result in injury or disease.

Air toxics risk assessments commonly look at two types of exposures and their associated toxic outcomes:

- Repeated or extended exposure to relatively low concentrations of air toxics over long periods of time (**chronic exposures**) that may result in **chronic health effects** (e.g., diseases like cancer or recurring respiratory ailments); and
- Infrequent exposure to relatively high concentrations of air toxics over short periods of time (**acute exposures**) that may result in the expression of either near term **acute health effects** (which can range from mild effects, such as reversible eye irritation, to extreme effects, such as loss of consciousness or sudden death), or long term effects (chronic effects).

### 3.3.2 Air Toxics Risk Assessment: The Process

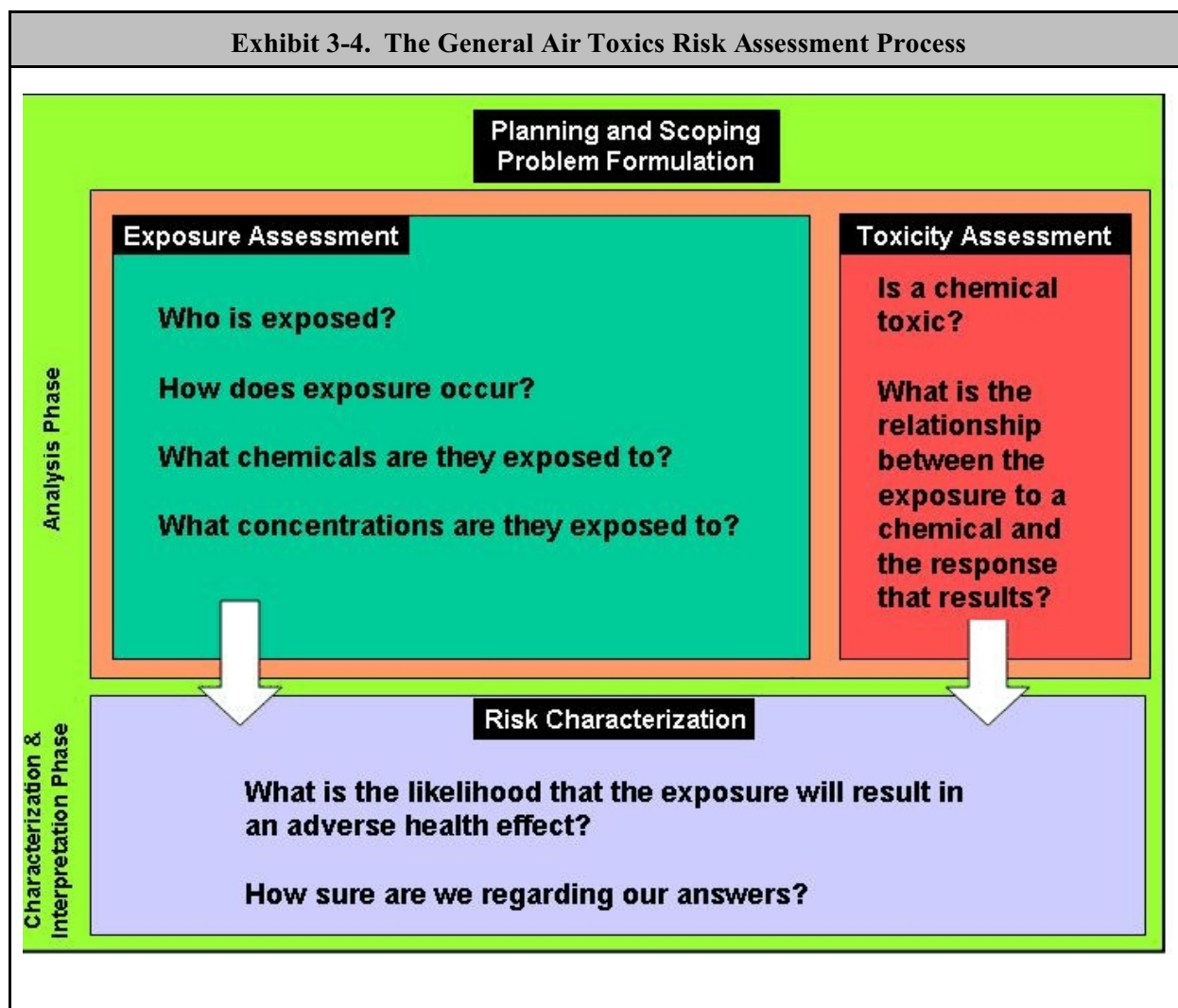
The illustration and narrative overview in the previous section (Exhibit 3-3) describes what may happen when toxic chemicals are released to the air and how those releases can result in adverse health outcomes in people. This picture and narrative description comprise a **conceptual model** of how releases of air toxics may pose risks to people. It is a conceptual model because it provides a picture (or “model”) of our “concept” of what may happen in the real world when toxic chemicals are released to the air. The conceptual model provides a starting point for estimating risks posed by those releases. However, in addition to a conceptual model (in this case, a simple picture), there is a need for a defined process to quantify relationships among the conceptual model components in order to generate numeric risk estimates. Exhibit 3-4 outlines the major steps in the process that EPA uses to perform a risk assessment:

- Planning, scoping, and problem formulation;
- Analysis, which includes exposure assessment and toxicity assessment; and
- Risk characterization.

With the addition of an explicit planning and scoping step (which should always be done for any systematic investigation), Exhibit 3-4 encompasses the same features as espoused by the National Academies in the Red and Blue books described previously. The National Academies’ process has been redrawn in Exhibit 3-4 to better clarify how the risk assessment is actually done in the air toxics arena.

It is useful to think of this figure as a “roadmap” to how air toxics risk assessments are performed. The roadmap breaks air toxics risk assessment down into four manageable elements, each of which are described briefly below and in detail in subsequent chapters. Note, however, that all of these steps are inter-related and usually require refinement throughout the risk assessment process. A helpful starting place is to think of these as “separate steps.”

Exhibit 3-4. The General Air Toxics Risk Assessment Process



### 3.3.2.1 Planning, Scoping, and Problem Formulation

Any human health risk assessment should begin with **planning and scoping**. Properly planning and scoping the risk assessment at the beginning of the project is critical to the success of the overall effort. Good planning and scoping clearly articulates the assessment questions; states the quantity and quality of data needed to answer those questions; provides in-depth discussion of how assessors will do the analysis; outlines timing and resource considerations, as well as product and documentation requirements; and identifies who will participate in the overall process from start to finish and what their roles will be. Poor planning and scoping will almost certainly lead to an assessment that does not answer the correct questions, does not provide a supportable basis for risk management decision-making, and wastes significant amounts of time, resources, and good will. The planning and scoping process needs to recognize, to the extent possible, important data gaps and uncertainties and the measures needed to address these problems. Where the extent of data gaps and their potential impacts on the risk assessment are not fully understood, the planning process may be iterative, with decision points specified during the analytical phase (see below) that are contingent on the results of data gathering efforts or sensitivity/uncertainty analyses.

During **problem formulation**, the planning and scoping team generally makes initial decisions about the scope of the risk assessment (e.g., size of the study area, what emission sources and chemicals are to be considered); the appropriate level of detail and documentation; trade-offs between depth and breadth in the analysis; quality assurance and quality control requirements; analytical approaches to be used (modeling vs. monitoring); and the staff and monetary resources to commit. Problem formulation results in two important products: the conceptual model and the analysis plan.

- The **study-specific conceptual model** is similar to the generic conceptual model (Exhibit 3-3); however, for an actual assessment the conceptual model explicitly identifies the physical boundaries of the study area; the potential emission sources and air toxics they are emitting that the risk assessment will consider; the location and composition of potentially exposed populations; the fate/transport mechanisms by which those populations may be exposed; the routes of exposures that may be occurring; and the expected health outcomes to be evaluated. The study-specific conceptual model is developed as both a picture and a written description of how air toxics emissions may be affecting the study area. As the assessment moves forward, the assessment team members will use the model as a guide, but they also routinely refine the model as they learn more about the study area. For example, the initial study-specific conceptual model may include a deposition element. If subsequent modeling or monitoring suggests this fate and transport mechanism is unimportant, the assessors will revise the conceptual model.
- The **analysis plan** will guide the remainder of the assessment. It lays out in detail how the elements of the conceptual model are going to be studied. In developing the analysis plan, it is important to include provisions for tiered or iterative analyses, as discussed in Sections 3.2.3 and 3.3.5.

### 3.3.2.2 Analysis Phase

The analysis phase is the process in which analysts apply risk assessment approaches to evaluate the problem at hand. It consists of two main components: exposure assessment and toxicity assessment.

An **exposure assessment** is conducted to characterize the potentially exposed population, the chemicals of potential concern, identify exposure pathways and routes of exposure, and estimate the exposure. This includes estimating or measuring concentrations of air toxics in the environment and evaluating how nearby populations interact with the contaminated media.

In the exposure assessment, the risk assessment team will refine the initial conceptual model by providing detailed information about the study area (e.g., physical description, meteorology, source locations and detailed characteristics, population demographics and locations, the

#### What is “Study-Specific?”

Air toxics risk assessments can be designed to evaluate a wide range of air toxics release scenarios. For example, a risk assessment might look at the impact of one emission point at a factory on a nearby population or it might look at the combined impact of hundreds of sources on a large urban area.

This reference manual uses the term “study-specific” to mean the specific geographic area and populations under study, along with the emission sources included in the scope of the study.

exposure pathways under study). The exposure assessment also is the analytic step in which the magnitude, frequency, and duration of human exposures are quantified. For example, one of the main outcomes of an air toxics exposure assessment is an estimate of the concentration of air toxics in the air at the point where human contact occurs (the EC). Assessors usually estimate this value with either a computer program (a **model**) or by physically taking samples of air and measuring air toxics concentrations in a laboratory (a **monitor**). When there are concerns about exposure pathways other than inhalation, assessors may use different models or monitoring strategies to estimate or measure concentrations of air toxics in soil, water, or foods.

The **toxicity assessment** component of the risk assessment process considers: (1) the types of adverse health effects associated with exposure to the chemicals in question, and (2) the relationship between the amount of exposure and resulting response. Toxicity assessment for air toxics generally consists of two steps:

- **Hazard identification** is the process of determining whether exposure to a chemical can cause an adverse health effect (e.g., cancer, birth defect, etc.), as well as the nature and strength of the evidence of causation and circumstances in which these effects occur (e.g., inhalation/ingestion, repeated exposure over a long period/single exposure over a short period, etc.).
- **Dose-response assessment** is the process of quantitatively characterizing the relationship between the dose of the contaminant and the incidence of adverse health effects in the exposed population. As information on dose at the site in the body where the response occurs is rarely available, various factors and models are used to predict the dose metric from estimates of exposure (the inhalation exposure concentration or oral intake). From this quantitative dose-response relationship, toxicity values are derived for use in risk characterization.<sup>(d)</sup> Most toxicity assessments are based on studies in which toxicologists expose animals to chemicals in a laboratory and extrapolate the results to humans. For some chemicals, information from actual human exposures is available (usually from workplace exposure studies).

Although air toxics risk assessors need to understand the underlying scientific basis and uncertainties associated with toxicity values, they will usually rely on toxicity values already developed and available in the literature. A list of default screening level toxicity values that EPA recommends for the 188 HAPs is in Appendix C. The most up-to-date list is at <http://www.epa.gov/ttn/atw/toxsource/summary.html>.

### 3.3.2.3 Risk Characterization

The **risk characterization** summarizes and combines outputs of the exposure and toxicity assessments to characterize risk, both in quantitative (numerical) expressions and qualitative (descriptive) statements. Chemical-specific exposure-response information is mathematically combined with modeled or monitored contaminant levels and other information regarding how exposure occurs to give numbers that represent the likelihood that the exposure may cause an

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<sup>d</sup>Toxicity values are numerical expressions of the relationship between a given level of exposure to an air toxic and adverse health impacts. The two most common toxicity values for inhalation exposures are the upper-bound inhalation unit risk estimates (IURs) for cancer effects and reference concentrations (RfCs) for non-cancer effects (which include uncertainty factors). Chapter 12 provides a more detailed discussion of toxicity values.

adverse health outcome. Per the Agency's *Policy for Risk Characterization*,<sup>(7)</sup> this likelihood is evaluated both with regard to a "central tendency" of exposure estimates and "high end" estimates. The risk characterization also includes a thorough **uncertainty analysis** for each step of the entire risk assessment process in order to provide the risk manager with an understanding of which elements of the assessment are most uncertain, the magnitude and direction of the effect (higher or lower) that the various uncertainties have on the risk estimates and in some cases, a quantitative analysis of uncertainty. Often the uncertainty analysis is a narrative that reflects the assessor's best professional judgment. Other analyses, however, may require a more quantitative approach to evaluating uncertainty.

The product of the risk assessment is a written report that provides all of the analyses performed to assess exposure, identify toxicity values, characterize risk, and assess and present uncertainty. It is critical that the risk assessment only provide the factual basis of why the assessment was done, how it was done, what the answers are, and the uncertainties associated with those answers. That is not to say that the risk assessment should not provide an analysis of differing scientific opinions on any number of the elements of the risk assessment. It does, however, preclude the assessment from discussing items more appropriately considered under risk management (e.g., cost or technical feasibility of mitigation alternatives). The presentation also must be clear and provide enough details so future readers will find the overall assessment process, including critical assumptions, to be fully transparent.

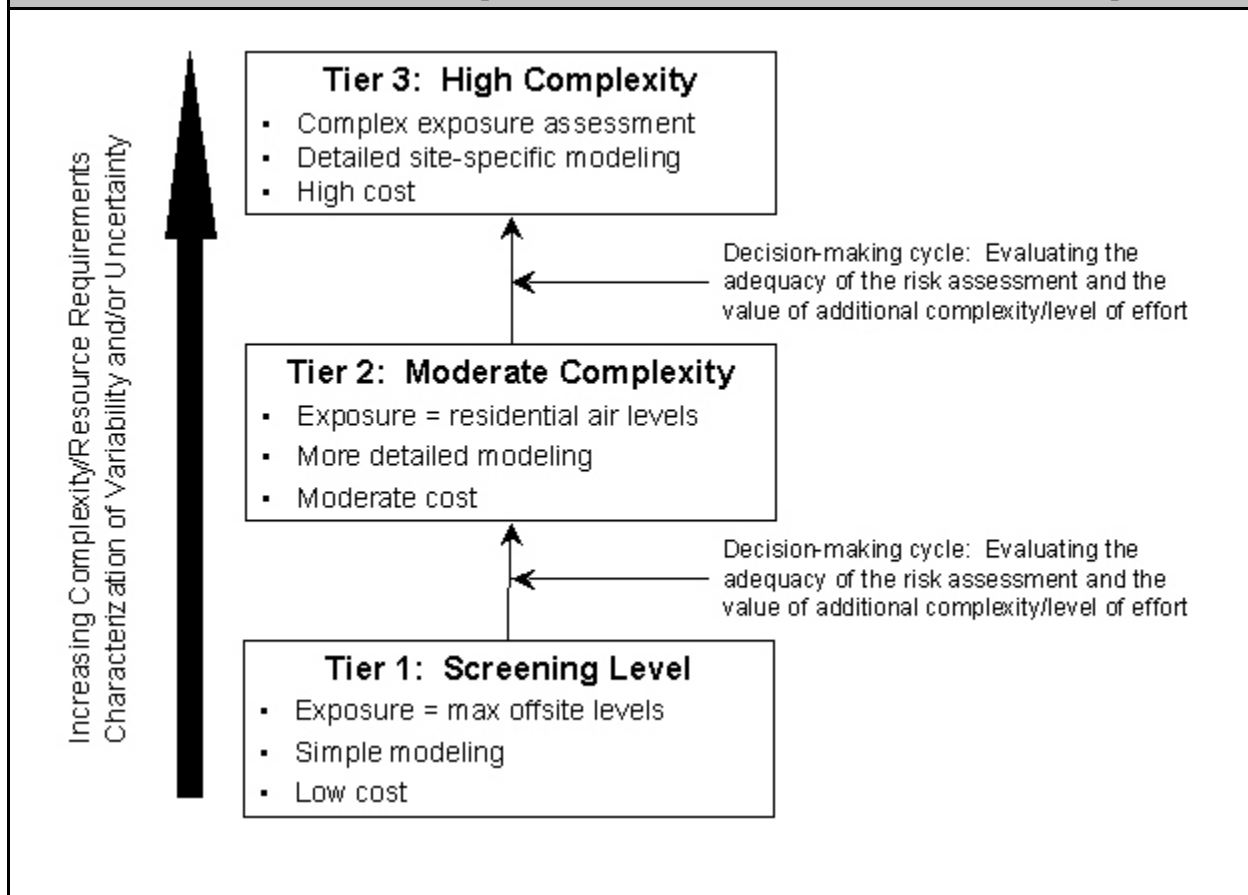
### 3.3.3 Tiered Assessment Approaches

Various EPA guidance documents and the Air Program's *Residual Risk Report to Congress* have recommended tiered approaches to risk assessments.<sup>(8)</sup> A tiered approach is a process for a systematic, informed progression from a relatively simple to a more complex risk assessment approach. Essentially, the approach begins with an analysis that includes few study-specific data and many conservative assumptions. This process generally results in a very conservative answer (and is likely to be fairly uncertain), but may demonstrate, with relatively little effort, that the sources being assessed pose insignificant risk. If such an approach indicates that the risk appears to be relatively high, assessors pursue a higher tier of analysis to determine if the risk is a realistic concern or an artifact of the lower tier's conservative assumptions. The higher level of analysis reflects increasing complexity and, in many cases, will require more time and resources. Higher tiers also reflect increasing characterization of variability and/or uncertainty in the risk estimate, which may be important for making risk management decisions.

Exhibit 3-5 illustrates a generalized representation of the tiered risk assessment concept. Central to the concept of the tiered approach is an iterative process of evaluation, deliberation, data collection, work planning, and communication aimed at deciding:

- Whether or not the risk assessment, in its current state, is sufficient to support the risk management decision(s); and
- If the assessment is determined to be insufficient, whether or not progression to a higher tier of complexity (or refinement of the current tier) would provide a sufficient benefit to warrant the additional effort.

### Exhibit 3-5. Generalized Representation of the Tiered Risk Assessment Concept



The deliberation cycle also provides an opportunity to evaluate the direction and goals of the assessment as new information becomes available. It may include evaluations of both scientific and policy information.

This representation, which provides an example of a tiered assessment process consistent with that described in the *Residual Risk Report to Congress*,<sup>(8)</sup> depicts three tiers of analysis. Each successive tier represents more complete characterization of variability and/or uncertainty as well as a corresponding increase in complexity and resource requirements.

- **Tier 1** is represented as a relatively simple, screening-level analysis using conservative exposure assumptions (e.g., receptors are located in the area with the highest estimated concentrations) and relatively simple modeling (e.g., a model that requires few inputs, most of which can be “generic,” yet conservative).
- **Tier 2** is represented as an intermediate-level analysis using more realistic exposure assumptions (e.g., use of actual receptor locations) and more detailed modeling (e.g., a model that requires additional site-specific inputs).
- **Tier 3** is represented as an advanced analysis using probabilistic techniques such as Monte Carlo analysis (see Part VII of this reference manual for a discussion of these techniques) and more detailed and/or intensive modeling.

This representation does not imply that there is a clear distinction between Tiers 1, 2, and 3. For example, a series of refinements in a Tier 1 analysis might be indistinguishable from a Tier 2 analysis, or a Tier 2 analysis could incorporate probabilistic techniques.

This representation also notes the decision-making cycle that occurs between each tier. In this cycle, the existing risk assessment results are evaluated to determine whether they are sufficient for the risk management decision, and if not, what refinements to the risk assessment are needed (including moving up to the next tier).

While the tiered risk assessment concept usually contains three tiers of complexity (as in Exhibit 3-5), these three tiers are best thought of as points along a spectrum of increasing complexity and detail in the risk assessment. The important focus is the specific ways in which a given risk assessment is refined in successive iterations, rather than whether or not it would be considered Tier 1, 2, or 3.

### **3.4 Uncertainty and Variability in Air Toxics Risk Assessment**

Risk assessment is based on a series of questions that the assessor asks about available scientific information that is relevant to human health and/or ecological risk. Each question calls for analysis and interpretation of the studies, selection of the concepts and data that are most scientifically reliable and most relevant to the problem at hand, and conclusions regarding the question presented. For example, in the exposure assessment, through the use of modeling and/or monitoring, the risk assessor asks what is known about the principal environmental fate and transport of contaminants and the patterns and magnitudes of human or ecosystem exposures. The toxicity assessment asks what is known about the ability of an air toxic to cause cancer or other adverse health effects in humans, laboratory animals, or wildlife species and what is known about the biological mechanisms and dose-response relationships underlying any effects observed in the laboratory or in epidemiology studies. The risk characterization integrates information from the preceding components of the risk assessment and synthesizes an overall conclusion about estimated risk that is complete, informative, and useful for risk managers.<sup>(7)</sup>

Air toxics risk assessments make use of many different kinds of scientific concepts and data (e.g., exposure, toxicity, epidemiology, ecology), all of which are used to characterize the estimated risk in a particular environmental context. Informed use of scientific information from many different sources is a central feature of the risk assessment process. Highly accurate information is often not available for many aspects of a risk assessment. However, since **scientific uncertainty** is inherent in the risk assessment process, and risk managers often must make decisions using assessments that are not as definitive in all important areas as would be desirable, it is important that the most current and complete information that is available be used to support decision making. Risk assessors and decision makers must understand that it may be necessary to revise risk estimates and to alter decisions in light of new information.

Risk assessments also incorporate a variety of professional judgements (e.g., which models to use, where to locate monitors, which toxicity studies to use as the basis of developing dose-response values). Risk managers therefore need to understand the strengths and the limitations of each assessment and to communicate this information to all participants and the public.

This section provides an overview of **uncertainty** and **variability**, two critically important characteristics of risk assessment that need to be understood and described at some level in every air toxics risk assessment. It describes several sources of uncertainty and variability in air toxics risk assessments, discusses approaches for describing and analyzing uncertainty and variability, and describes how uncertainty and variability are often addressed at different tiers of the risk assessment process.

A full discussion of this subject, including quantitative techniques for uncertainty analysis, is beyond the scope of this reference manual. Risk assessment is an evolving discipline, and improvements in scientific understanding and techniques will continue to provide new avenues and insights into uncertainty and variability analysis. Because this manual is intended as an introduction to risk assessment approaches and tools, our discussion focuses on relatively simplistic, deterministic risk assessment techniques (i.e., Tier 1 approaches to risk characterization that lead to single value estimates of risk). Readers are encouraged to consult the references at the end of this Chapter for additional information about uncertainty analysis in the risk assessment process.

### 3.4.1 Distinguishing Uncertainty and Variability

**Variability** refers to true heterogeneity or diversity. For example, among a local community that is exposed to an air toxic originating from the same source, and with all people breathing the same contaminant concentration in ambient air, the risks from inhalation of the contaminated air will still vary among the people in the population. This may be due to differences in exposure (i.e., different people have different exposure frequencies and exposure durations), as well as differences in response (e.g., differences in metabolic processes of chemical uptake into target organs). Differences among individuals in a population are referred to as inter-individual variability, while differences for one individual over time (e.g., change in sensitivity to air toxics with aging, illness) are referred to as intra-individual variability.

**Uncertainty** occurs because of a lack of knowledge. For example, we can be very certain that different people are exposed to contaminated air for different time periods, but we may be uncertain about how much variability there is in these exposure durations among the people in the population. Data may not be available concerning the amount of time specific people spend indoors at home, outdoors near home, or in other “microenvironments.”

Uncertainty can often be reduced by collecting more and better data, while variability is an inherent property of the population being evaluated. Variability can be better characterized with more data, but it cannot be reduced or eliminated. Often, however, it is difficult to distinguish between uncertainty and variability in a risk assessment, particularly if available data are limited. For that reason, in many cases variability can be treated as a type of uncertainty in the risk assessment.

Uncertainty is an inherent characteristic of each step of the risk assessment process. Assessing uncertainty in risk assessment is an involved process because of the complex nature of the risk assessment process itself (i.e., risk assessment is a combination of a variety of data gathering and analytical processes, each with their own associated uncertainties). Specifically, risk assessment requires the integration of the following:

- Information on emissions of air toxics into the environment;
- Information on the fate and transport of air toxics, in a variety of different and variable environments, by processes that are often poorly understood or too complex to quantify completely;
- Information on the potential for adverse health effects in humans and/or ecosystems, often extrapolated from surrogate animal studies; and
- Information on the likelihood of adverse effects in a human population that is highly variable genetically, as well as factors such as age, activity level, lifestyle, and underlying disease.

Uncertainty, when applied to the process of risk assessment, is defined as “a lack of knowledge about specific factors, parameters, or models.”<sup>(9)</sup> Such uncertainties affect the confidence of any risk estimates that were developed for individuals exposed to the substances in question.<sup>(10)</sup> It is important to keep in mind that many parameter values (e.g., emissions rates) may be *both* uncertain and variable. Also, the presence of uncertainty in risk assessment does not imply that the results of the risk assessment are wrong, but rather that the risks cannot be estimated beyond a certain degree of confidence.

The relatively simple, deterministic (i.e., single value estimate) approach outlined in this reference manual generally relies on a combination of point values – some which may be set at protective (i.e., high end) levels and some which may be set at typical (i.e., central tendency) levels. The result is a point estimate of exposure, and risk that falls at some percentile within the full distributions of exposure and risk. The degree of conservatism in high end risk estimates depends on the combination of input values selected.<sup>(11)</sup>

One of the key purposes of the uncertainty analysis is to provide an understanding of where the estimate of exposure, dose, or risk is likely to fall within the range of possible values. Often this is expressed as a subjective confidence interval (one based on incomplete data supplemented by professional judgment) within which there is a high probability that the estimate will fall. A related analysis, termed “sensitivity analysis” or “analysis of uncertainty importance,” is often performed to identify the relative contribution of the uncertainty in a given parameter value (e.g., emission rate, ingestion rate) or model component to the total uncertainty in the exposure or risk estimate. This is often used either to identify which parameter values should be varied to provide high-end vs. central-tendency risk estimates, or to identify parameter values where additional data collection (or modeling effort) can increase the confidence in the resulting risk estimate.

### 3.4.2 Sources of Uncertainty in Air Toxics Risk Assessment

Although other taxonomies are sometimes used, sources of uncertainty in risk assessment are often divided into four categories (variability is sometimes included as a fifth category).<sup>(12)</sup>

- **Scenario uncertainty** occurs when information to fully define exposure and/or risk is missing or incomplete. This may include descriptive errors regarding the magnitude and extent of chemical exposure or toxicity, temporal and spatial aggregation errors, incomplete analysis (i.e., missing exposure pathways), and potential mis-specification of the exposed population or exposure scenario.
- **Model uncertainty** is associated with all models used in all phases of a risk assessment, including (1) animal models used as surrogates for evaluating human carcinogenicity, (2)

dose-response models, (3) computer models used to predict the fate and transport of chemicals in the environment, and (4) models used to estimate exposures for populations of concern. Model uncertainty also is sometimes referred to as specification uncertainty.

Computer models are simplifications of reality that use mathematical approximations to describe the most important processes governing the modeled relationships, while excluding what are believed to be less important processes, or processes that are too complex to be easily approximated. The risk assessor needs to consider the potential importance, in consultation with the modeler, of the level of detail and comprehensiveness of the models being used, because specific processes may have important impacts on uncertainty in some instances and not in others. A similar problem can occur when a model that is applicable under average conditions is used for a case in which conditions differ from the average. In tiered analyses, resource considerations and the level of precision required to support decision making may enter into considerations of model selection. Model uncertainty may be particularly important in multipathway analyses, because the modeling effort is much more complex (as compared to inhalation analyses). In addition to air quality modeling, multipathway analyses involve analysis of the transfer of air toxics from the air to other media (e.g., soil, sediment, water); the subsequent movement of the air toxics between these media (e.g., soil runoff to surface water); uptake and metabolism by biota; and subsequent ingestion by humans and wildlife. Uncertainties are associated with all of these analytical steps.

Model uncertainty is often difficult to deal with quantitatively. It is rarely possible to directly evaluate the merits of competing models, either due to resource constraints, or because direct comparisons are inherently complex (e.g., the models may take different input parameters, and produce outputs that are not directly comparable). Statistical methods (Bayesian analyses) can sometimes be used to combine the results of different models, but these approaches are often complex, and generalizability to specific cases is hard to predict. Thus, model selection tends to be based primarily on professional judgement and cost/complexity considerations.

- **Parameter Uncertainty** refers to the limitations in the modelers' ability to estimate precise values for certain parameters (variables) in the chosen models. It is a generic term that in common usage can refer either to variability or uncertainty, and generally indicates a situation where a given variable may take a range of values, rather than a single point estimate. Parameter uncertainty is generally addressed in risk assessment through gathering additional data, sensitivity analysis, or probabilistic modeling (discussed in Section 3.3.4).
- **Decision-rule uncertainty** is a type of uncertainty associated with policy and other choices made during the risk assessment. For example, the number of chemicals of potential concern (COPC) evaluated at a given tier of assessment may be reduced through use of a toxicity-weighted or risk-based screening analysis. In this example, the decision rule could be something like "Calculate the toxicity weighted emission for each chemical in the emissions inventory, rank the scores from highest to lowest and, starting with the highest score and working down, select as COPCs those chemicals that contribute to 99 percent of the cumulative toxicity weighted sum." This type of judgment introduces uncertainties about the contribution of the omitted air toxics to overall exposure or risk. As another example, risk managers may decide to select as chemicals for risk reduction efforts (i.e., the Chemicals

of Concern or COCs) only those COPCs that, individually, pose a risk above some specified level (e.g., one per million general population lifetime cancer risks). In this case, the decision rule would be “COCs are those COPCs which have a risk, on an individual chemical basis, of one in one million or greater.” For any given risk assessment, some or all of these practices may be questioned, either on technical grounds (e.g., a risk number has been generated, but it is highly uncertain) or for policy reasons. The risk assessor needs to be sensitive these considerations when planning, conducting, and reporting the results of the risk assessment.

### **3.4.3 Sources of Variability in Air Toxics Risk Assessment**

As noted previously, variability refers to true heterogeneity or diversity that occurs within a population or sample. Factors that lead to variability in exposure and risk include variability in contaminant concentrations in an environmental medium (e.g., air, water, soil) and differences in other exposure parameters such as ingestion rates and exposure frequencies.

Temporal and spatial variability in contaminant concentrations is often a very important aspect to consider in air toxics risk assessments. Spatial variability arises from many factors, including the release forms, physical and chemical dilution and transformation processes, and physical characteristics of the source or surrounding environment. Ecological receptors and humans may exhibit spatial variability in their contact with an exposure medium. Likewise, temporal variability can result from a variety of factors. For example, a source may only emit a chemical at specific times during the year (e.g., during the processing of a batch of product).

Meteorological changes between seasons also can cause variable exposure (even though source emissions remain relatively constant). Because variability is an intrinsic property of the quantities being evaluated, it cannot be reduced by data gathering or refinements in models. However, understanding and/or analysis of variability are still important, especially during problem formulation. For example, it may be thought that certain air toxic emission source characteristics or potentially exposed populations are very heterogeneous and that a more robust description of the numbers and types of people at different risk levels is necessary to meet risk management decision goals

Confusion often arises about whether data are describing variability or uncertainty. For example, consider a group of 10,000 office workers who spend part of the time indoors at home and part of the time indoors at work. To assess the fraction of time spent indoors at a home or the office, a randomly chosen group of 100 office workers are asked to fill out a survey (resources preclude surveying all 10,000 people). Once we have our data, we draw a frequency diagram of the number of workers who spend specified amounts of time indoors at home and at the office. The picture we get clearly shows that different people spend different amounts of time inside at home and at the office – there is variability in the parameter for this population.

However, is our picture of variability correct (i.e., how certain are we that we have a good picture of the true variability of all 10,000 people)? Since we did not survey every possible worker and because some of the workers may have given incorrect responses, we have to admit to ourselves that there is probably some amount of uncertainty as to whether our frequency diagram is an accurate representation of variability in full worker population. In other words, we have developed an expression of variability that we think is uncertain. But only having a sense that our picture of variability may not be an accurate representation may not be enough (knowing just how uncertain our estimate of variability is may be important in our risk assessment).

Fortunately we have a variety of methods to look at the uncertainty in just one parameter (e.g., how variable is time spent indoors versus outdoors) and in the combination of parameters to provide estimates of exposure and risk. We can, for example, look at our data to see if patterns of time use vary for different subgroups of workers, or we can look for “outliers” (individuals with unusual patterns of indoor/outdoor time use). Alternatively, we could gather data from a larger sample of workers. Any of these would decrease the level of uncertainty in worker behavior, by providing more accurate representations of the variability of time usage for more clearly defined categories of workers. The newly developed worker categories would then be included in the exposure modeling.

#### 3.4.4 Characterizing Uncertainty and Variability

Ideally, one would like to carry through the risk assessment, in a quantitative fashion, the uncertainty associated with each element in order to characterize the overall uncertainty associated with the final risk estimates. However, this is not always possible (because data are extremely limited) and, in some cases, may not be necessary (when all reasonable modeling assumptions and parameter values lead to the same recommendation). Nevertheless, it is always a good idea to provide some level of uncertainty analysis (be it qualitative, semi-quantitative, or quantitative). For example, one important use of uncertainty characterization can be to identify areas where a moderate amount of additional data collection might significantly improve the risk assessment, and hence the decision on the need for risk reduction or the risk reduction strategy to be used.

- **Qualitative characterization.** In a qualitative uncertainty analysis, a description of the uncertainties in each of the major elements of the risk analysis is provided, often with a statement of the estimated magnitude of the uncertainty (e.g., small, medium, large) and the impact the uncertainty might have on the risk element (e.g., the uncertainty is large and risk estimate is likely underestimated due to this element).
- **Quantitative characterization.** When appropriate, quantitative approaches to the uncertainty analysis are used to better characterize the uncertainty associated with the risk assessment. In this case, the first step is usually to characterize the probability distributions for key input parameter values (either using measured or assumed distributions). The second step would be to propagate parameter value uncertainties through the analysis using analytic (e.g., first-order Taylor series approximation) or numerical (e.g., Monte Carlo simulation) methods, as appropriate. Analytic methods might be feasible if there are a few parameters with known distributions and linear relationships. Numerical methods (e.g., Monte Carlo simulation) can be suitable for more complex relationships. “Two-dimensional” Monte Carlo analyses may be used where separate estimates of uncertainty and variability are available for some or all variables. Specific approaches are likely to be highly variable depending on the nature of the assessments being performed. Examples of approaches applied to a variety of assessments are provided in the reference list at the end of this chapter in Exhibit 3-8 (Hope, 1999; Moore et al., 1999; Smith, 1994).
- Both qualitative and quantitative uncertainty characterization is subject to scope-related limitations and uncertainty. For example, ecological risk assessments that are limited to primary effects evaluation for organisms or populations are uncertain with regard to secondary effects for communities or ecosystems. Similarly, human health assessments that

are restricted to the HAPs may ignore exposures and potential effects from other chemicals in the same emissions. Such uncertainties persist regardless of the assessment's refinement level (Tier). Their communication provides important contextual information for decision making.

Guidance developed by the National Council on Radiation Protection and Measurements<sup>(13)</sup> provides useful insights as to when to perform a quantitative uncertainty analysis in environmental risk assessments (Exhibit 3-6).

Exhibit 3-6. When to Perform a Quantitative Uncertainty Analysis
<p><b>Quantitative uncertainty analysis is NOT recommended when:</b></p> <ul style="list-style-type: none"> <li>• Conservative, screening-level calculations indicate that the risk from potential exposure is clearly below regulatory or other risk levels of concern;</li> <li>• The cost of an action to reduce exposure is low; and/or</li> <li>• Data for characterizing the nature and extent of contamination or exposure are inadequate to permit even a bounding estimate (an upper and lower estimate of the expected value).</li> </ul>
<p><b>Quantitative uncertainty analysis IS recommended when:</b></p> <ul style="list-style-type: none"> <li>• An erroneous result in the exposure or risk estimate may lead to large or unacceptable consequences;</li> <li>• Whenever a realistic rather than a conservative estimate is needed; and/or</li> <li>• When it is important to identify those assessment components for which additional information will likely lead to improved confidence in the estimate of exposure or risk.</li> </ul>
<p><i>Source: NCRP. 1996. <sup>(13)</sup></i></p>

### 3.4.5 Tiered Approach to Uncertainty and Variability

Building on the approach outlined in Exhibit 3-6, the following description provides one possible tiered approach to deciding when and how to perform an uncertainty analysis.<sup>(14)</sup>

**Single-Value Estimates of High-End and Central Tendency Risk.** This approach starts with simple risk estimates using both representative and more conservative scenarios, models, and input values, using point estimates to represent each of the major parameters. This “deterministic” approach, which is described extensively in this document, may provide sufficient information for the risk management question being addressed. For example, if risks for a suitably defined high-end receptor are below levels of concern, then no additional uncertainty analysis (or risk analysis) may be needed to support a risk management decision. It is important to recall, however, that using single values for inputs, essentially ignores uncertainty and variability – information that may be very important for risk managers and the public.

Despite some limitations, single-value estimates or point estimates are an important tool in the risk assessment process. Single-value estimates are particularly useful as a screening tool to identify situations in which even highly conservative assumptions about exposure and other model parameters indicate low risk. (Note that EPA risk assessors are directed to provide, in Agency risk assessments, information about the range of exposures derived from exposure

scenarios and on the use of multiple risk descriptors [e.g., central tendency, high end of individual risk, population risk, important subgroups, if known] consistent with terminology in the Guidance on Risk Characterization, Agency risk assessment guidelines, and program-specific guidance.<sup>(7)</sup>)

**Qualitative Evaluation of Model and Scenario Sensitivity.** Where the single-value high-end and central tendency point estimates do not provide sufficient information to make a risk management decision, qualitative analyses can be conducted to determine the range of values within which the risk estimate is likely to fall and the major factors that contribute to uncertainty. The sensitivity of the high-end and central tendency estimates to the plausible range of values for various parameters can usually be evaluated by conducting a manageable number of case studies using different parameter values and observing the resulting changes in risks. If scenario or model specification turns out to strongly affect risk estimates, a more refined analysis (see below) may be necessary. These may include Bayesian or decision-tree models.

**Quantitative Sensitivity Analysis of High-End or Central Tendency Estimates.** The risk assessor may want to evaluate the sensitivity of the point estimates of risks to variability and uncertainty in model input parameters. This may be done through sensitivity analysis or through the use of more detailed probabilistic methods (see Chapter 31). If sensitivity analyses are used, care must be taken to ensure that the combinations of parameter values that have the greatest impact on risks are identified.

**Full Quantitative Characterization of Uncertainty and Uncertainty Importance.** For many risk assessments, the systematic sensitivity analyses can provide sufficient information to provide reasonable confidence in the risk estimate. If they do not, the next step is explicit probability modeling, which is described in Chapter 31. Using such approaches, uncertainty and variability distributions can be defined for the major parameter values used in the derivation of the risk estimates. This approach is referred to as **parameter uncertainty analysis** and includes the following steps:<sup>(15)</sup>

- **Define the assessment endpoint** (i.e., the specific measure being evaluated). Examples would include an estimate of exposure concentration, hazard index, or a quantitative estimate of individual cancer risk.
- **List all potentially important uncertain parameters.** Include additional parameters, if necessary, to represent uncertainty in the assessment approach itself.
- **Specify the maximum conceivable range of possibly applicable values for each parameter with respect to the endpoint being assessed.**
- **For this range, specify a probability distribution for the parameter.** The probability distribution quantitatively expresses the state of knowledge about alternative values for the parameter (i.e., defines the probability that the true value of the parameter is located in various sub-intervals of the indicated range). These may include statistical distributions (e.g., “normal” or other distributions derived from data) or simpler approximations (triangular distributions defined by high, medium, and low values).

- **Determine and account for dependencies that are suspected to exist among parameters.**  
For example intake rate may not be independent of age or body weight.
- **Using either analytical or numerical procedures, propagate the uncertainty in the model parameters to produce a probability distribution for the assessment endpoint.**  
This results in the development of a probability distribution function (PDF) representing the state of knowledge for the endpoint.
- **Derive quantitative statements of uncertainty in terms of a probability or confidence interval about the assessment endpoint.**
- **Identify parameters according to their relative contribution to the overall uncertainty in the prediction of the value of the assessment endpoint.**
- **Present and interpret the results of the analysis.**

A full quantitative characterization of uncertainty requires a number of assumptions, including:

- The most important sources of uncertainty and variability are identified;
- The assumed probability distributions are correct; and
- The assumed dependence structure for different sources of uncertainty or variability is correct.

A comprehensive quantitative analysis may be a daunting task, particularly if a large number of sources, chemicals, receptors, exposure pathways, and endpoints, are of concern. Furthermore, the difficulty in justifying a large number of distributional assumptions (often based on professional judgement) needed for an uncertainty analysis might make such an analysis in itself unreliable.

In practice, the number of “tiers” available to the risk assessor may be limited. Often the practical choice is between using simple “screening” models (e.g., SCREEN3), and highly refined, fully parameterized modeling packages (e.g., ISCST3). In such cases, it may be easier to do a highly refined analysis with the state-of-the art models than to incrementally improve on the screening methods.

### **3.4.6 Assessment and Presentation of Uncertainty**

The assessment and presentation of uncertainty is a very important component of the risk characterization. Based on the amount of information about sources and emissions and the degree of uncertainty associated with estimates of risk, decision-makers will weigh the importance of the risk estimates in the eventual decision. As noted previously, when the uncertainty analysis is qualitative in nature, a description of the uncertainties in each of the major elements of the risk analysis is usually described, often with a statement of the estimated magnitude of the uncertainty (e.g., small, medium, large) and the impact the uncertainty might have on the risk element (e.g., the uncertainty is large and risk estimate is likely underestimated). Important uncertainties to discuss include, but are not limited to:

- Scope issues such as the choice of air toxics, receptors, or endpoints that are evaluated in the assessment and the choice of air quality or multimedia models used to characterize exposure;
- Data quality issues, such as the quality of available sampling, emissions inventory, or toxicity data;
- Uncertainties inherent in the toxicity values for each substance used to characterize risk; and
- Uncertainties that are incorporated in the risk assessment when exposures to several substances across multiple pathways are summed.

When the analysis is more quantitative in nature, the description of uncertainty generally is separated into two parts:

- The first part is a summary of the values used to estimate exposure and risk (including model inputs), the range of these values, the midpoint or other descriptive values, and the value used to estimate exposure.
- The second part is a narrative discussion that identifies which variables or assumptions used in the risk assessment have the greatest potential to affect the overall uncertainty in the exposure assessment.

Chapter 13 provides additional discussion of how to assess and present uncertainty in an air toxics risk assessment. Exhibit 3-7 provides additional references on uncertainty analysis.

#### **Example of a Six-step Process for Producing a Quantitative Uncertainty Estimate**

Finkel (1990)<sup>(12)</sup> presents another example of a quantitative uncertainty analysis process:

1. Define the measure of risk (such as deaths, life-years lost, maximum individual risk [MIR], or population above an “unacceptable” level of risk). More than one measure of risk may result from a particular risk assessment; however, the uncertainty may be quantified or reached individually.
2. Specify “risk equations” that present mathematical relationships that express the risk measure in terms of its components. This step is used to identify the important variables in the risk estimation process.
3. Generate an uncertainty distribution for each variable or equation component. These uncertainty distributions may be generated by using analogy, statistical inference techniques, expert opinion, or a combination of these.
4. Combine the individual distributions into a composite uncertainty distribution.
5. Re-calibrate the uncertainty distributions. Inferential analysis could be used to “tighten” or “broaden” particular distributions to account for dependencies among the variables and to truncate the distributions to exclude extreme values.
6. Summarize the output clearly, highlighting the important risk management implications. Address specific critical factors, including (1) the implication of supporting a point estimate produced without considering uncertainty; (2) balance the costs of under- or over-estimating risks; and (3) unresolved scientific controversies, and their implications for research.

### Exhibit 3-7. Additional References on Uncertainty Analysis

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